

Attorney Docket No. 960296.99179
Applicants: Thomson et al.
Filed: 25 July 2003
U.S. Application No.: 10/627,245
Art Unit: 1636
Date of Office Action: 31 December 2007
Examiner: Daniel M. Sullivan

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application.

Listing of Claims:

1. (currently amended) A method for testing an agent for effect on human cardiac cells comprising the steps of
culturing aggregates of approximately 500-800 undifferentiated human embryonic stem cells to produce embryoid bodies;
~~deriving atrial-, ventricular- and nodal cardiomyocyte cell types after~~ differentiating the embryoid bodies in *in vitro* culture for between 40 and 95 days of embryoid bodies derived from human embryonic stem cells to derive atrial-, ventricular- and nodal cardiomyocyte cell types;
piercing a single cardiomyocyte with an electrode so that the transmembrane action membrane of that cardiomyocyte can be electrically measured;
measuring the transmembrane action potential of the single cardiomyocyte;
assessing the transmembrane action potential of the cardiomyocyte to characterize the cardiomyocyte as to the cell type of the human heart that the action potential most resembles among the cell types selected from the group consisting of ventricular, atrial and nodal cell types;
exposing the cardiomyocyte to the agent; and
observing whether the action potential of the cardiomyocyte changes after the exposure to the agent.
2. (cancelled).
3. (previously presented) The method of claim 1 wherein the deriving is conducted by permitting the human embryonic stem cells to form embryoid bodies and wherein the measuring includes impaling the single cardiomyocyte within an embryoid body with the electrode.

4-6. (cancelled).

7. (currently amended) A method for testing an agent for its effect on the electrical properties of the HERG channel in human cardiac cells comprising the steps of
culturing aggregates of approximately 500-800 undifferentiated human embryonic stem cells to produce embryoid bodies;

~~deriving atrial-, ventricular- and nodal cardiomyocyte cell types after differentiating the embryoid bodies in~~ in vitro culture for between 40 and 95 days ~~of embryoid bodies derived from human embryonic stem cells to derive atrial-, ventricular- and nodal cardiomyocyte cell types;~~

inserting an electrode into the interior of a single cardiomyocyte in culture in order to be able to measure the transmembrane action potential of the cardiomyocyte;

measuring the duration of the transmembrane action potential of the cardiomyocyte;

assessing the transmembrane action potential of the cardiomyocyte to characterize the cardiomyocyte as to the cell type of the human heart that the action potential most resembles among the cell types selected from the group consisting of ventricular, atrial and nodal cell types;

exposing the cardiomyocyte to the agent; and

observing whether the action potential duration is changed by the agent, as would be the case if the HERG channel is altered.

8. (cancelled).

9. (original) The method of claim 7 wherein the culturing is conducted by permitting the human embryonic stem cells to form embryoid bodies and wherein the measuring includes impaling an embryoid body with an electrode.

10. (currently amended) A method for testing an agent for its likelihood of triggering delayed after depolarization events in human cardiac cells comprising the steps of
culturing aggregates of approximately 500-800 undifferentiated human embryonic stem cells to produce embryoid bodies;
~~deriving atrial, ventricular and nodal cardiomyocyte cell types after differentiating the embryoid bodies in~~ in vitro culture for between 40 and 95 days ~~of embryoid bodies derived from human embryonic stem cells to derive atrial-, ventricular- and nodal cardiomyocyte cell types;~~
inserting an electrode into the interior of a single cardiomyocyte in culture in order to be able to measure the transmembrane action potential of the cardiomyocyte;
obtaining a chart of the transmembrane action potential of the cardiomyocyte over time;
assessing the transmembrane action potential of the cardiomyocyte to characterize the cardiomyocyte as to the cell type of the human heart that the action potential most resembles among the cell types selected from the group consisting of ventricular, atrial and nodal cell types;
exposing the cardiomyocyte to the agent; and
observing whether a delayed after polarization event is triggered by the agent.

11. (cancelled).

12. (original) The method of claim 10 wherein the culturing is conducted by permitting the human embryonic stem cells to form embryoid bodies and wherein the measuring includes impaling an embryoid body with an electrode.

13. (currently amended) A method for testing an agent for its likelihood of triggering long QT syndrome in patients by testing human cardiac cells comprising the steps of
culturing aggregates of approximately 500-800 undifferentiated human embryonic stem cells to produce embryoid bodies;

~~deriving atrial, ventricular and nodal cardiomyocyte cell types after differentiating the embryoid bodies in in vitro culture for between 40 and 95 days of embryoid bodies derived from human embryonic stem cells to derive atrial-, ventricular- and nodal cardiomyocyte cell types;~~

separately inserting an electrode into the interior of several single cardiomyocytes in the culture in order to be able to measure the transmembrane action potential of the cardiomyocytes;

obtaining a chart of the transmembrane action potential of a plurality of the cardiomyocytes over time;

assessing the transmembrane action potential of the cardiomyocytes to characterize the cardiomyocytes as to the cell type of the human heart that the action potential most resembles among the cell types selected from the group consisting of ventricular, atrial and nodal cell types;

exposing the cardiomyocytes to the agent; and

observing whether action potential duration is prolonged, as an indicator of the risk of long QT syndrome by the agent in any of the cardiomyocytes.

14. (cancelled).

15. (original) The method of claim 13 wherein the culturing is conducted by permitting the human embryonic stem cells to form embryoid bodies and wherein the measuring includes impaling embryoid bodies with an electrode.

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16. (currently amended) A method for testing an agent for effect on human cardiac cells comprising the steps of

culturing aggregates of approximately 500-800 undifferentiated human embryonic stem cells by in vitro culture to produce embryoid bodies;

selecting amongst the embryoid bodies for embryoid bodies which demonstrate the presence of atrial-, ventricular- and nodal cardiomyocyte cell types;

piercing the embryoid body to place a fine electrode inside a single cardiomyocyte within the embryoid body so that the transmembrane action membrane of that cardiomyocyte can be electrically measured;

measuring the transmembrane action potential of the single cardiomyocyte;

assessing the transmembrane action potential of the cardiomyocyte to characterize the single cardiomyocyte as to the cell type of the human heart that the action potential most resembles among the cell types selected from the group consisting of ventricular, atrial and nodal cell types;

exposing the cardiomyocyte to the agent; and

observing whether the action potential of the cardiomyocyte changes after the exposure to the agent.